Remarks/Arguments:

Upon entry of this amendment, claims 1, and 3-19 will be pending in this application. Claims 10-19 are withdrawn as directed to non-elected subject matter, claim 2 is canceled herein, and claims 1, 4-6, and 8-9 are amended herein, without the addition of new matter. Any subject matter cancellation is made without prejudice to one or more continuing applications.

35 U.S.C. §112, First Paragraph

Claims 1-9 stand rejected as allegedly failing to comply with the written description requirement. The office action states that a divider is required to separate the flow tracks, but is not described by the specification. Applicants respectfully traverse the rejection.

Claim 1 has been amended to recite that the indicator zones are positioned such that the liquid for any one flow track does not flow through more than one indicator zone. Support for the amendment can be found throughout the specification, for example, at page 6, lines 1-5, and claim 2. Applicants submit that it is not necessary that a physical barrier be present to separate the flow tracks as alleged in the office action. The subject matter is adequately described and withdrawal of the rejection is warranted.

35 U.S.C. §112, Second Paragraph

Claims 1-9 stand rejected as allegedly indefinite. It is believed that the amendments to claims 1, 4, 5, 6, 8, and 9 obviate the rejection as applied to these claims. With respect to the rejection of claim 4, it is submitted that the blood group antigens are recognized by the International Society of Blood Transfusion and would otherwise be readily understood by those of skill in the art. For the Examiner's convenience, Applicants have attached a copy of page 230 from the textbook Human Blood Groups, a copy of pages 111-112 of The Blood Group Antigen Facts Book, and a citation from http://en.wikipedia.org/wiki/Human_blood_group_systems, to illustrate the accepted nature of the antigen designations.

With respect to the rejection of claim 3, the office action indicates that it is not clear whether the zones are arranged in the shape of the letters. Applicants submit that claim 3 recites that the indicators zones are arranged in a diagonal V-, W-, M-, or N-*shape*. Claim 3 is thus clear on its face. The rejection is improper and should be withdrawn.

With respect to the rejection of claim 7, the office action objects to the description of the sealing element. Applicants submit that the sealing element is described throughout the

specification, see for example, pages 9-10 and Figures 4-14. Claim 7 is thus clear on its face. The rejection is improper and should be withdrawn.

35 U.S.C. §102(b)

Claims 1-9 stand rejected as allegedly anticipated by WO 88/08534 ("May"). Applicants respectfully traverse the rejection.

May describes an analytical test device with a casing constructed of moisture-impervious solid material containing a dry porous carrier and a sample receiving member. May also describes a plurality of detection zones arranged in series on the porous solid phase material, through which the aqueous liquid sample can pass progressively (page 11, lines 22-24). May does not, however, teach or suggest a plurality of detection zones arranged in parallel as alleged. In contrast, May discloses only test strips arranged in parallel such that a single application of liquid sample to the device initiates sample flow in the discrete bodies simultaneously. In May's disclosure, there is only one flow track on one test strip (a membrane).

May does not disclose a device comprising a membrane with an application zone, at least two indicator zones and at least one absorption region wherein at least two different flow tracks are present, and wherein the indicator zones are positioned such that the liquid for any one flow track does not flow through more than one indicator zone. Furthermore, the indicator zones of May are so arranged that the test liquid of a flow track flows through more than one indicator zone (page 4, lines 4-13).

Due to its transverse-arranged indicator zones, a simultaneous detection of a plurality of analytes is thus not possible using May's device if the analyte is erythrocyte bound antigens due to the existence of a physical barrier between the indicator zones. According to May, different analytes can only be simultaneously tested using different test strips. Therefore, May does not anticipate the claimed invention.

35 U.S.C. §103(a)

Claims 1-9 stand rejected as allegedly obvious over U.S. 7,303,923 ("Hardman") in view of May. Applicants respectfully traverse the rejection.

In addition to lacking an absorption region, the device described by Hardman differs from the claimed device in several other ways. For example, the porous material in the Hardman device is a channel system. Thus, when a plurality of analytes are to be tested, the bibulous compartment always has a central body connected to a plurality of channels (see, *e.g.*,

col. 4, lines 57-61 and col. 6, lines 61-67; and, Figures 2-3). Thus, the Hardman device requires separate membranes, and a physical barrier to separate the channels is a prerequisite for simultaneous detection of a plurality of analytes. Additionally, the flow tracks described by Hardman are not substantially parallel, but are instead Y-shaped. In contrast, the instant device utilizes a single membrane with multiple flow tracks that are substantially parallel, and the indicator zones are positioned such that the liquid for any one flow track does not flow through more than one indicator zone. A physical barrier is not required for simultaneous detection of a plurality of analytes.

May does not remedy the deficiencies of Hardman. As explained above, May does not teach or suggest a plurality of detection zones arranged in parallel on a single membrane, and thus does not permit the testing of multiple analytes using a single test strip. In addition, the use of multiple membranes by May requires a physical barrier to separate the flow tracks.

The cited art, when considered individually, or in the combination set forth in the office action does not teach or suggest all of the limitations of the claimed invention. A *prima facie* case for obviousness thus has not been established. Accordingly, withdrawal of the rejection is warranted.

Obviousness Double Patenting

Claims 1-9 stand provisionally rejected on the grounds of nonstatutory obviousness-type double patenting over claims 1-3, 7, 11-12, and 14-15 of co-pending application U.S. 10/563,861. Applicants note the rejection and will address the rejection upon the indication of allowable subject matter. Applicants request that the rejection be held in abeyance.

The foregoing is a *bona fide* attempt to advance the prosecution of this application to allowance. Applicants respectfully request reconsideration and withdrawal of the various rejections in light of the amendments and remarks made herein. A notice of allowance is requested.

Respectfully submitted,

June 26, 2008

/Brian A. Cocca/

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Brian A. Cocca, Ph.D., Reg. No. 58,583
Attorneys for Applicant

Attachments:
(1) Wikipedia "Human blood group systems"

(2) Marion E. Reid et al. "The Blood Group Antigen Facts Book" pages 111-112

(3) Geoff Daniels "Human Blood Groups 2d.ed." page 230

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Human blood group systems

From Wikipedia, the free encyclopedia

The International Society of Blood Transfusion (ISBT) currently recognises 29 major blood group systems (including the ABO and Rh systems).[1] Thus, in addition to the ABO antigens and Rhesus antigens, many other antigens are expressed on the red blood cell surface membrane. For example, an individual can be AB RhD positive, and at the same time M and N positive (MNS system), K positive (Kell system) and Le^a or Le^b positive (Lewis system). Many of the blood group systems were named after the patients in whom the corresponding antibodies were initially encountered.

The ISBT definition of a major blood group system is where one or more antigens are "controlled at a single gene locus or by two or more very closely linked homologous genes with little or no observable recombination between them".[2]

Contents

Blood Grouping Procedure

Blood is composed of cells suspended in a liquid. The liquid portion is the plasma, from which therapeutic fractions and derivatives are made.

Suspended in the plasma are three types of cells:

- **Red cells** carry oxygen
- **White cells** fight infection
- **Platelets** stop bleeding in injuries

The most common type of grouping is the ABO grouping. Red Blood Cells have a protein coat on their surface which distinguishes them. According to this blood is divided into four groups:

- A (A protein is present)
- B (B protein is present)
- AB (A and B proteins are present)
- O (no proteins are present)

There are subtypes under this grouping (listed as A1, A2, A1B or A2B...) some of which are quite rare. Apart from this there is another protein which plays an important part in the grouping of blood. This is called the Rh factor. If this is present, the particular blood type is called positive. If it is absent, it is called negative. Thus we have the following broad categories:

- A1 Negative (A1 -ve)
- A1 Positive (A1 +ve)
- A1B Negative (A1B -ve)
- A1B Positive (A1B +ve)

- A2 Negative (A2 -ve)
- A2 Positive (A2 +ve)
- A2B Negative (A2B -ve)
- A2B Positive (A2B +ve)
- B Negative (B -ve)
- B Positive (B +ve)
- O Negative (O -ve)
- O Positive (O +ve)

Information Courtesy: Indian Red Cross Society, Tamil Nadu Branch.

How is a blood group categorized as rare?

A rare blood type is any blood type that is difficult to find. A blood type is classified as rare when more than 200 donors have to be screened to find one compatible donor with blood of that type. In the "ABO" system, all Blood belongs to one of four major group: A, B, AB, or O. But there are more than two hundred minor blood groups that can complicate Blood transfusions. These are known as rare blood Types. About one person in 1,000 will inherit a rare blood type. Normally expressed in a letter or two, with maybe a plus or a minus, these few persons read their blood type in an extensive series of letters in addition to their 'ABO' type designation. (E.g.:AB +ve, O -ve, A1 -ve, etc. are the rare types)

Table

ISBT N°	Common name	abbreviation	Epitope or carrier, notes	Locus
001	ABO	ABO	Carbohydrate (N-Acetylgalactosamine, galactose). A, B and H antigens mainly elicit IgM antibody reactions, although anti-H is very rare, see the Hh antigen system (Bombay phenotype, ISBT #18).	9
002	MNS	MNS	GPA / GPB (glycophorins A and B). Main antigens M, N, S, s.	4
003	P	P1	Glycolipid.	22
004	Rhesus	RH	Protein. C, c, D, E, e antigens (there is no "d" antigen; lowercase "d" indicates the absence of D).	1
005	Lutheran	LU	Protein (member of the immunoglobulin superfamily). Set of 21 antigens.	19
006	Kell	KEL	Glycoprotein. K_1 can cause hemolytic disease of the newborn (anti-Kell), which can be severe.	7
007	Lewis	LE	Carbohydrate (fucose residue). Main antigens Le^a and Le^b - associated with tissue ABH antigen secretion.	19
008	Duffy	FY	Protein (chemokine receptor). Main antigens Fy^a and Fy^b. Individuals lacking Duffy antigens altogether are immune to malaria caused by *Plasmodium vivax* and *Plasmodium knowlesi*.	1
009	Kidd	JK	Protein (urea transporter). Main antigens Jk^a and Jk^b.	1

010	Diego	DI	Glycoprotein (band 3, AE 1, or anion exchange). Positive blood is found only among East Asians and Native Americans.	17
011	Yt or Cartwright	YT	Protein (AChE, acetylcholinesterase).	7
012	XG	XG	Glycoprotein.	X
013	Scianna	SC	Glycoprotein.	1
014	Dombrock	DO	Glycoprotein (fixed to cell membrane by GPI, or glycosyl-phosphatidyl-inositol).	12
015	Colton	CO	Aquaporin 1. Main antigens Co(a) and Co(b).	7
016	Landsteiner-Wiener	LW	Protein (member of the immunoglobulin superfamily).	19
017	Chido/Rodgers	CH/RG	C4A C4B (complement fractions).	6
018	Hh/Bombay	H	Carbohydrate (fucose residue).	19
019	Kx	XK	Glycoprotein.	X
020	Gerbich	GE	GPC / GPD (Glycophorins C and D).	2
021	Cromer	CROM	Glycoprotein (DAF or CD55, regulates complement fractions C3 and C5, attached to the membrane by GPI).	1
022	Knops	KN	Glycoprotein (CR1 or CD35, immune complex receptor).	1
023	Indian	IN	Glycoprotein (CD44 adhesion function?).	11
024	Ok	OK	Glycoprotein (CD147).	19
025	Raph	MER2	Transmembrane glycoprotein.	11
026	JMH	JMH	Protein (fixed to cell membrane by GPI).	6
027	Ii	I	Branched (I) / unbranched (i) polysaccharide.	6
028	Globoside	P	Glycolipid.	3
029	GIL	GIL	Aquaporin 3.	9

References

1. ^ Table of blood group systems. International Society of Blood Transfusion (October 2006). Retrieved on 2006-11-14.
2. ^ ISBT Committee on Terminology for Red Cell Surface Antigens. Terminology Home Page. Retrieved on 2006-11-14.

External links

- ISBT Table of blood group antigens within systems Updated October 2006
- BGMUT Blood Group Antigen Gene Mutation Database
- Blood group The Faculty of Applied Sciences, University of the West of England

Retrieved from "http://en.wikipedia.org/wiki/Human_blood_group_systems"
Categories: Blood | Transfusion medicine | Hematology

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THE BLOOD GROUP ANTIGEN FactsBook

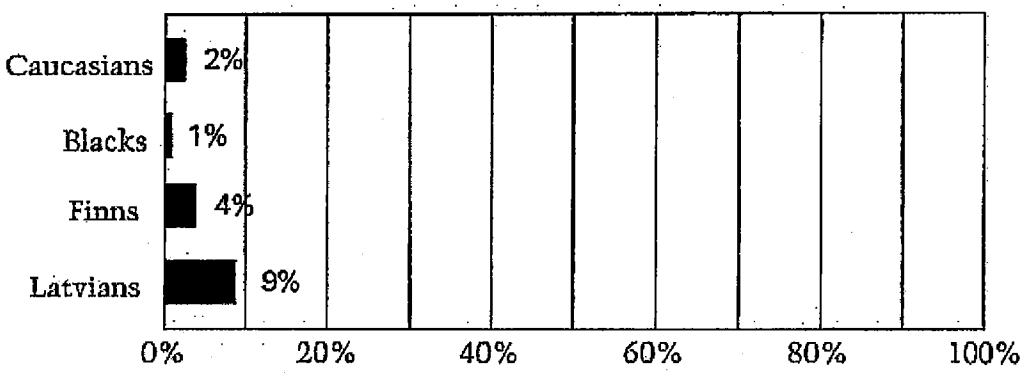
Marion E. Reid
Christine Lomas-Francis

C^w ANTIGEN

Terminology

ISBT symbol	RH8
ISBT number	004.008
Other name	Willis, rh^{w1}

Occurrence



Antithetical antigen

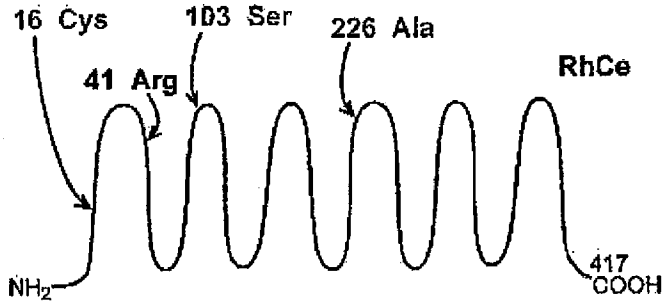
C^X (RH9); MAR (RH51)[1]

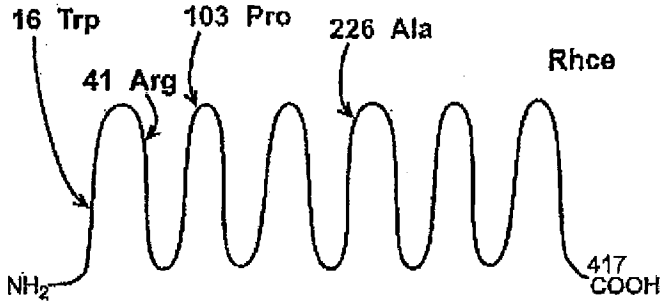
Expression

Cord RBCs	Expressed
Altered	Weaker on DC^w-

Molecular basis associated with antigen[2]

Nucleotide: G at bp 122.
C^w- has amino acid Gln at residue 41 of the RhCe and Rhce polypeptide. The wild type gene has A at bp 122. In addition, the RhCe polypeptide has Cys at residue 16 (associated with C antigen [RH2]) from nucleotide $G^{48} \rightarrow C$.





Effect of enzymes and chemicals on intact RBCs

Ficin/Papain	Resistant (↑↑)
Trypsin	Resistant (↑)
α-Chymotrypsin	Resistant (↑)
Pronase	Resistant (↑↑)
Sialidase	Resistant
DTT 200 mM	Resistant
Chloroquine (RT)	Resistant
Acid	Resistant

In vitro characteristics of alloantibody

Immunoglobulin class	IgG and IgM
Optimal technique	RT, IAT, enzymes
Complement binding	No

Clinical significance of alloantibody

Transfusion reaction	Mild to severe/immediate and delayed
HDN	Mild to moderate

Comments

Anti-C^w are often naturally occurring and found in multispecific sera. Most C^w+ are C+; rare examples are C–. C^w has been associated with D(C)C^we, D(C)C^wE, (C)C^we, (C)C^wE, DC^w– and C^wce haplotypes.

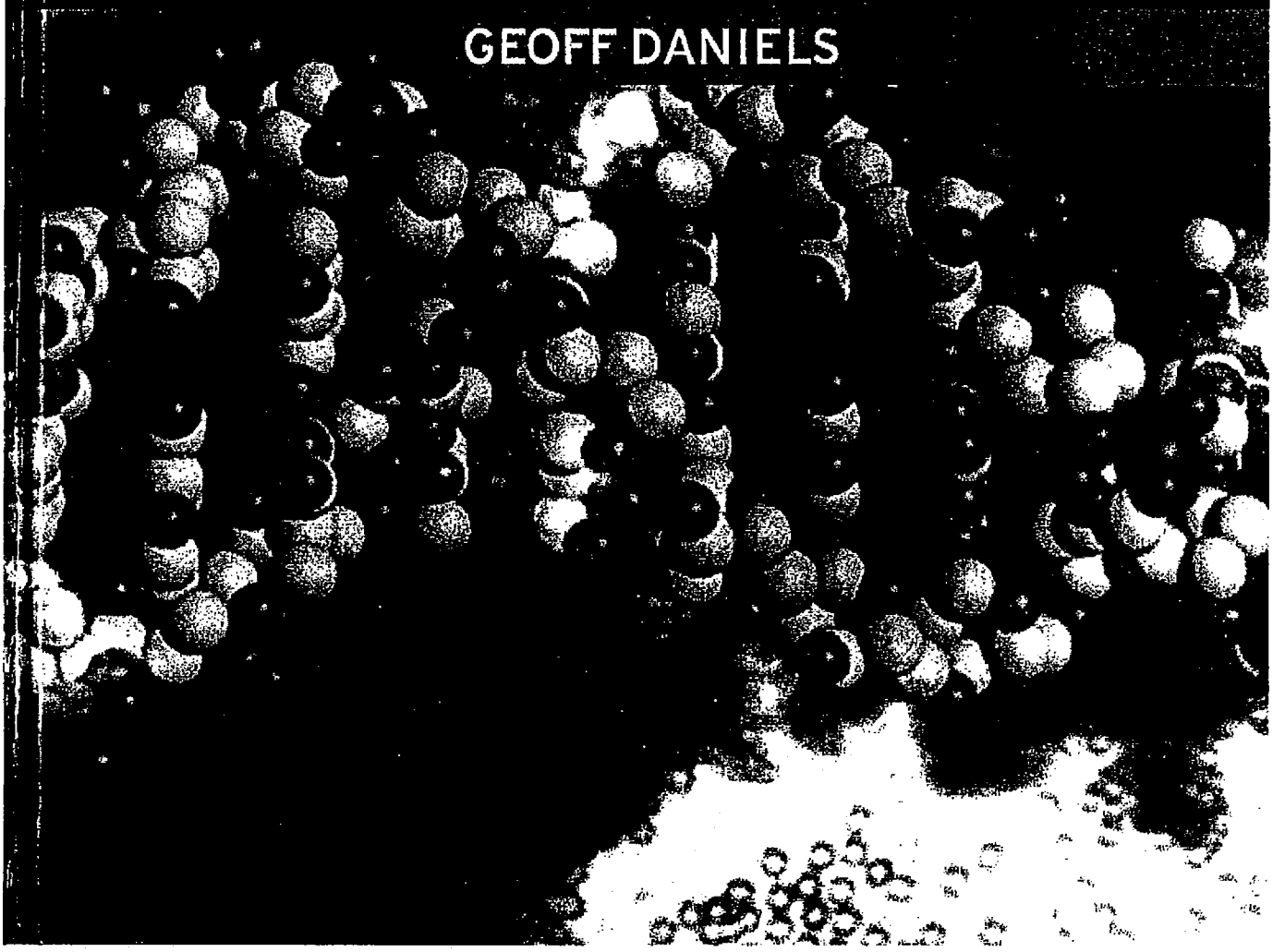
References

1 Sistonen, P. et al. (1994) Vox Sang. 66, 287–292.
2 Mouro, I. et al. (1995) Blood 86, 1196–1201.

Human Blood Groups

SECOND EDITION

GEOFF DANIELS



5.12.1 C^w (RH8)

Callender and Race [392] found the first example of anti-C^w in the serum of a DCe/DCe patient who had been transfused with DCe/DCe C^w+ red cells. In an English population C^w has an occurrence of 2.6% [13]; similar frequencies are found in most other northern European and white American populations [14]. The highest frequency of C^w (7–9%) has been found in Latvians, Lapps, and Finns [30]; in most other populations it is very much lower [14, 21].

C^w+ red cells are almost always C+, but the C antigen associated with C^w is weaker than normal C, though recognition of this weakness depends on the anti-C used. Although C^w is usually produced by a *DCe* haplotype, C^w associated with *dCe* [392], *dCE* [393], and *DCE* [394] have also been found. A person with apparently normal DCC^we/dce red cells made anti-C that did not react with DCC^we/dce or dCC^we/dce cells [395]. Similar antibodies have been detected in the sera of DCC^we/DCC^we and DCC^we/DcE individuals [396,397].

Studies with ^{125}I-labelled human monoclonal anti-C^w provided the following estimates of C^w sites per red cell: DCC^we/DCC^we 32 000; DCC^we/DCe 15 200; DCC^we/DcE 19 800; DCC^we/dce 15 300; dCC^we/dce 26 200 [398]. Similar studies with monoclonal anti-C did not reveal any obvious reduction in C antigen density in C^w+ cells compared with C^w– cells [398].

Very rarely, C^w is produced by *RHCE* that produces c and e [391,399,400]. In one individual with C^w+C–c+ red cells, the cells were also D– and G– (dcC^we/dce) (G. Wittman, R. Zimmermann, M. Wallace, P. Tippett, personal communication). C^w is usually produced by a *Ce* allele of *RHCE* encoding Arg41; C^w associated with c is produced by a *ce* allele encoding Arg41 and Cys16 [391]. CC^we and cC^we alleles therefore have exons 1 of identical sequence (see Table 5.10) and cC^we could have arisen by recombination between CC^we (exon 1) and *ce* (exons 2–10) alleles of *RHCE*. The DC^w– haplotype, which produces C^w but no C, c, E, or e, is described in Section 5.15.4.

Anti-C^w is not an uncommon antibody and often results from no known red cell immunizing stimulus. One in 1100 pregnant Manitoban women had anti-C^w [401]. Anti-C^w has been responsible for several cases of HDN, but this has seldom been severe (reviewed in [401]). Bowman and Pollock [401] conclude that neonatal deaths as a result of anti-C^w reported in 1947 [402] probably resulted from kernicterus caused by absence of exchange transfusion. PCR-based methods for predicting fetal C^w phenotype are useful in the management of potential HDN caused by anti-C^w [391,403].

5.12.2 C^x (RH9)

Like C^w, C^x is usually produced by a *DCe* haplotype that produces abnormal C. C^x+ red cells react with some, but not all, anti-C. Two very rare haplotypes also encode C^x: dCC^xe [30] and, in four of 513 unrelated Somalis, dcC^xe^s, which produces c, V, and VS, but no C or ce [404].

Seven C^x-positives were found among 5919 (0.12%) British donors [405,406] and 202 were found among 70 503 (0.29%) Americans [407]. C^x has a much higher incidence in Finland: 37 of 2060 (1.8%) Finns were C^x+ [390].

The first anti-C^x caused mild HDN, as have other examples since [405,406]. Some anti-C^x appear to be 'naturally occurring' [408]. Anti-C in the serum of a transfused DCC^xe/dce patient reacted with most C+ cells, including DCC^we/dce cells, but not with DCC^xe/dce, DCC^xe/DcE, or DCC^xe/DCC^xe cells [409].

5.12.3 MAR (RH51)

Anti-MAR was found in a Finnish woman whose red cells were C^w+C^x+D+C+c–E–e+ and who was probably heterozygous DCC^we/DCC^xe [390]. Testing of 10 045 Finnish donors revealed 21 MAR-negatives: nine were C^w+C^x– (probably C^w/C^w), three were C^w–C^x+ (C^x/C^x), and nine were C^w+C^x+ (C^w/C^x). In eight families, all 20 children of MAR– parents were either C^w+ or C^x+. Anti-MAR reacted weakly with many examples of C^w+C^x– and C^w–C^x+ cells. It did not react with Rh_{null}, D––, or DC^w– cells. As C^w and C^x usually result from Gln41Arg and Ala36Thr substitutions in the RhCe protein, respectively [391], it is probable that both Gln41 and Ala36 are required for MAR expression.

Two other antibodies to high frequency antigens, produced in probable C^x [407] and C^w [410] homozygous women, resembled anti-MAR in their serological reactions. However, the antibody from the C^w homozygote reacted weakly with DCC^xe/DCC^xe cells